

**REMARKS**

Reconsideration is requested.

The specification has been amended to update the cross-reference to prior applications which was included with the Preliminary Amendment of June 27, 2003. The Examiner is requested to contact the undersigned in the event anything further is required in this regard. The Examiner is requested to confirm receipt in the Patent Office of the foreign priority document. The Examiner is requested to confirm the same has also been noted in a Bib. Data Sheet in the PTO IFW.

The Drawings filed February 9, 2007 include the nucleic acid "numbers" in each sheet of Figure 1. The Examiner's requirement for same in some of the sheets of Figure 1 appears to relate to Figures filed June 27, 2003, as opposed to the most recently-filed drawing sheets. The specification has been revised above to include in the brief description of the figures a statement of the correlation between the sequences of Figure 1 and the sequences of the Sequence Listing. Inclusion of same in the Figures is not believed to be required where the same information can and is now included in the specification as a further description of the Figure. Finally, the applicants note that the sequences of the claims find support for, example, in the specification and figures as follows: SEQ ID NOs: 279-313. Figure 1; SEQ ID NO: 75, page 28, HBPr75; SEQ ID NO:76, page 28, HBPr76; SEQ ID NO:77, Fig. 1D; SEQ ID NO:78, Fig. 1D; SEQ ID NO:80, Fig. 1D; SEQ ID NO:94, HBPr94, page 28; SEQ ID NO:105, HBPr105, page 28; SEQ ID NO:112, HBPr112, page 28; SEQ ID NO:134, HBPr134, page 29; SEQ ID NO:135, HBPr135, page 29; SEQ ID NO:140, Fig 1D; SEQ ID NO:148, Fig 1E; SEQ ID NO:153, Fig 1D; SEQ ID NO:154, Fig 1D; SEQ ID NO:165,

Fig 1D; SEQ ID NO:172, Fig 1D; SEQ ID NO:177, Fig 1D; SEQ ID NO:186, Figure 4; SEQ ID NO:193, Fig 1D; SEQ ID NO:204, Fig 1E; SEQ ID NO:208, Fig 1D; SEQ ID NO:213, Fig 1E; SEQ ID NO:216, Fig 1D; and SEQ ID NO:219 Fig 1D.

Acceptance of the drawings is requested.

The Examiner is requested to see the applicants Submission of December 20, 2006 in response to the Examiner's comments relating to the earlier-filed Information Disclosure Statement. Return of an initialed copy of the PTO 1449 Form filed December 20, 2006, pursuant to MPEP § 609, is requested.

A separate Information Disclosure Statement is attached. The cited "Other Documents" are being filed electronically and consideration and return of an initialed copy of the attached PTO 1449 Form are requested. The attached Information Disclosure Statement cites U.S. Patent Office file histories of co-pending application Serial Nos. 09/155,885; 10/453,792 and 11/802,328, as well as a related patent and published patent application document.

The claims have been amended to obviate the objection stated in §11. on page 4 of the Office Action dated December 14, 2006.

The Section 102 rejection of claims 15 and 16 over McDonough (EP 0569237A2) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

Th applicants understand the cited art to relate to a method to detect whether a sample comprises HBV. Probes are disclosed to detect unique sequences in the HBV genome which are capable to distinguish between the HBV and its known phylogenetic neighbors, see the summary of the invention. This is essentially different from the

presently claimed invention however which discloses a method to detect in a sample the presence or absence of a well-defined genotype HBV, here HBV A.

The Examiner is understood to suggest that the detection of HBV by detecting HBV<sub>adv</sub> as taught by McDonough is the same as detecting the *genotype* HBV A.

However, on the one hand nine *serotypes* have been described. Their nomenclature is based on the common "a" determinant in HBsAg and at least two mutually exclusive subdeterminants, "d" or "y", and "w" or "r". On the other hand, currently for HBV 8 genotypes have been described (A-H) based on an inter-genome divergence of 8% or more.

The conventionally classified serotypes are sometimes erroneously called genotypes. Genetic analysis has, however, revealed that the serotypes do not correspond with single *genotypes*, with several *serotypes* encoded by more than one *genotype* (see the attached table).

The cited document fails to teach each and every aspect of the claimed invention. Withdrawal of the Section 102 rejection is requested.

The Section 103 rejection of claims 15-17, 28 and 29 over McDonough, Maertens (WO 94/12670) and Ashton-Rickard (Journal Medical Virology 1989, November; 29(3); 196-203), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

The Examiner is understood to believe that the description of antigenically essentially residues in the immunodominant  $\alpha$  region of a *serotype* as described by Ashton-Rickardt would have made the finding of a probe to detect a *genotype* obvious. However, the Examiner is requested to appreciate that the cited art is describing

different targets achieved by different processes. Combining the cited Ashton-Rickardt publication with the general teaching of establishing whether HBV is present in a sample as disclosed by EP 0569237 would not have made the claimed invention obvious.

Maertens generally describes a method for genotyping various viruses whereunder HBV, but does not give any indication in which part of the genome the probes and primers should be construed. With the present invention both the region (HBsAg) and specific primer and probes have been disclosed to provide a method to establish whether genotype A is present or not in a sample, eventually combined with the presence of other genotypes.

Withdrawal of the Section 103 rejection is requested.

Rejoinder of previously-withdrawn subject matter and allowance of same with the pending active claims are requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required.

STUYVER, et al.  
Appl. No. 10/606,879  
June 14, 2007  
Amendment

Respectfully submitted,

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## Relationship between serological subtypes and genotypes

HBV genotype	HBsAg serotype	Geographical distribution
<b>A</b>	<b>adw2</b>	<b>Europe, N. America, Africa</b>
	<b>ayw1</b>	
<b>B</b>	<b>adw2</b>	<b>Far East</b>
	<b>ayw1</b>	<b>Far East</b>
<b>C</b>	<b>adrq</b>	<b>Pacific</b>
	<b>adr / ayr</b>	<b>Far East</b>
	<b>adw</b>	<b>Japan, Indonesia</b>
	<b>adr</b>	<b>Far East, Pacific</b>
<b>D</b>	<b>ayw4</b>	<b>USA</b>
	<b>ayw2 / ayw3</b>	<b>Worldwide</b>
<b>E</b>	<b>ayw4</b>	<b>Africa</b>
<b>F</b>	<b>adw2</b>	<b>S.America,</b>
	<b>Adw4</b>	<b>Polynesia, Alaska, C.- and S. America</b>
	<b>ayw4</b>	<b>S. America</b>
<b>H</b>	<b>Adw4</b>	<b>Central America</b>